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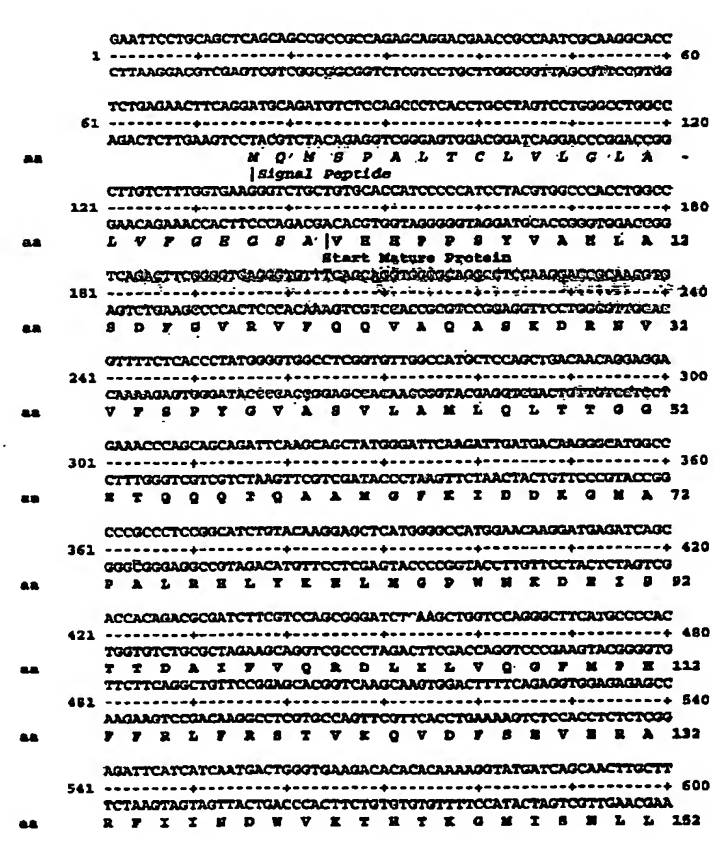
(54) Title: MODIFIED PLASMINOGEN ACTIVATOR INHIBITOR TYPE-1 AND METHODS BASED THEREON



(57) Abstract: The present invention is based upon the discovery that modified plasminogen activator inhibitor type-I (PAI-1) in which two or more amino acid residues that do not contain a sulfliydryl group have been replaced with amino acid residues that contain a sulfhydryl group and, therefore, forms intramolecular disulfide bonds, have increased in vivo half-life. Also disclosed are the modified PAI-1 proteins, derivatives and analogs thereof, specific antibodies, nucleic acid molecules and host cells. Methods for producing modified PAI-1, derivatives and analogs are also provided. The invention further relates to Therapeutics, pharmaceutical compositions and method of using the composition for treatment. The invention may be used to inhibit angiogenesis in a subject, thereby treating diseases or conditions associated with undesired angiogenesis and cell proliferation. Such conditions include psoriasis, chronic inflammation, tumor invasion and metastasis and conditions in which angiogenesis is pathogenic. The modified PAI-1 molecules of the present invention are useful for the treatment, prophylaxis, management and amelioration of cardiovascular diseases such as, but not limited to those that are related to hyerfibrinolysis, hemophilia, and vessel leakage syndrome.

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